09/12/017
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	Type	L #	Hits	Search Text	DBs	Time Stamp	Comments	Error Definition	Errors
1	IS&R	L1	4106	(("514/8") or ("530/395") or ("530/396") or ("530/399") or ("530/402") or ("530/404") or ("530/411")).CCLS.	USPAT	2000/09/06 08:29			0
2	BRS	L2	6276	lectin or selectin	USPAT	2000/09/06 08:29			0
3	BRS	L3	643	l1 and l2	USPAT	2000/09/06 08:34			0
4	BRS	L4	616	heparin-binding	USPAT	2000/09/06 08:34			0
5	BRS	L5	875	heparin adj binding	USPAT	2000/09/06 08:36			0
6	BRS	L6	15508	growth adj factor	USPAT	2000/09/06 08:36			0
7	BRS	L7	2698	fibroblast adj l6	USPAT	2000/09/06 08:37			0
8	BRS	L8	4245	epidermal adj l6	USPAT	2000/09/06 08:37			0
9	BRS	L9	2832	platelet adj derived adj l6	USPAT	2000/09/06 08:38			0
10	BRS	L10	6571	l4 or l5 or l7 or l8 or l9	USPAT	2000/09/06 08:38			0
11	BRS	L11	824	l1 and l10	USPAT	2000/09/06 08:40			0
12	BRS	L12	11427	glycosy1$	USPAT	2000/09/06 08:40			0
13	BRS	L13	75850	sugar	USPAT	2000/09/06 08:40			0
14	BRS	L14	32464	carbohydrate	USPAT	2000/09/06 08:41			0
15	BRS	L15	10613	saccharide	USPAT	2000/09/06 08:42			0
16	BRS	L16	24699	polysaccharide	USPAT	2000/09/06 08:42			0
17	BRS	L17	1847	glycosaminoglycan	USPAT	2000/09/06 08:42			0

	Type	L #	Hits	Search Text	DBs	Time Stamp	Comments	Error Definition	Errors
18	BRS	L18	111803	l12 or l13 or l14 or l15 or l16 or l17	USPAT	2000/09/06 08:45			0
19	BRS	L19	201	l10 with l18	USPAT	2000/09/06 08:45			0
20	BRS	L20	45	l1 and l19	USPAT	2000/09/06 08:46			0

CCXR:
530/395

ORPL:
Settineri, et al., Characterization of O-Glycosylation Sites in Recombinant
B-Chain of Platelet-derived Growth Factor Expressed in Yeast Using Liquid
Secondary Ion Mass Spectrometry, Tandem Mass Spectrometry and Edman Sequence
Analysis, Biomedican and Environmental Mass Spectrometry, 19:665, 1990.

prob not needed

USPT

US-CL-CURRENT: 435/69.1,435/69.6 ,530/380 ,530/402

see also 5,827,824
5,466,668

US-PAT-NO: 6063763
DOCUMENT-IDENTIFIER: US 6063763 A
TITLE: Protease-resistant thrombomodulin analogs
DATE-ISSUED: May 16, 2000
INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Light; David Richard	San Mateo	CA	N/A	N/A
Andrews; William H.	San Mateo	CA	N/A	N/A
Clarke; Jeffrey Homer	Pacifica	CA	N/A	N/A
Wydro; Robert Michael	Foster City	CA	N/A	N/A
Young; Patricia Ann	San Rafael	CA	N/A	N/A

US-CL-CURRENT: 514/12,435/69.1 ,435/69.6 ,530/380 ,530/402
ABSTRACT:
The present invention relates to the single-chain thrombomodulin ("TM") and analogs thereof that are not susceptible to cleavage by proteases and retain the biological activity of thrombomodulin, as well as methods of use in, for example, antithrombotic therapy. Novel proteins, nucleic acid gene sequences, pharmaceuticals and methods of inhibiting thrombotic activity are disclosed.
18 Claims, 5 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 4

DEPL:
259:12246-12251, which is incorporated herein by reference). In

DEPL:
259:12246-12251, which is incorporated herein by reference). In comparison to native thrombomodulin, preferred TM analogs have been modified to embrace the 6 epidermal growth factor [EGF]-like domains and may also contain the O-linked glycosylation and/or lectin domains.

not a clear teaching

CCXR:
530/402

USPT

US-CL-CURRENT: 514/2,514/8 ,530/350 ,530/380 ,530/829

US-PAT-NO: 5939390
DOCUMENT-IDENTIFIER: US 5939390 A
TITLE: Pharmaceutical composition
DATE-ISSUED: August 17, 1999
INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Flodgaard; Hans	Hellerup	N/A	N/A	DKX
Rasmussen; Poul Baad	Copenhagen .O	N/A	N/A	DKX

slashed.

US-CL-CURRENT: 514/12,514/2 ,514/8 ,530/350 ,530/380 ,530/829

ABSTRACT:

The present invention relates to a pharmaceutical composition for the prevention or treatment of diseases or conditions involving stress injury to cells, the composition comprising

(a) a lipid-containing substance having a lipid portion which is structurally identical with or analogous to a ceramide, conjugated to

(b) a protein capable of binding said lipid-containing substance in such a way that, when the conjugate is contacted with living cells, the lipid-containing substance activates a ceramide-activated protein phosphatase resulting in down-regulation of cellular metabolism, and

(c) a pharmaceutically acceptable diluent or carrier.

31 Claims, 2 Drawing figures
Exemplary Claim Number: 1

probably not needed

reducing
conditions), the protein being produced in the azurophil granules
of
polymorphonuclear leukocytes.

CLPR:
2. A composition according to claim 1, wherein the protein to
which the
lipid-containing substance is conjugated is a heparin-binding
protein which, in
glycosylated form, has an apparent molecular weight of 28 kD as
determined by
SDS-PAGE under reducing conditions, the protein being produced in
the azurophil
granules of polymorphonuclear leukocytes.

CLPV:
(b) a heparin-binding protein which, in glycosylated form, has an
apparent
molecular weight of 28 kD, the protein being produced in the
azurophil granules
of polymorphonuclear leukocytes and is capable of binding said
lipid-containing
substance in such a way that, when the conjugate is contacted
with living
cells, the lipid-containing substance activates a
ceramide-activated protein
phosphatase resulting in down-regulation of cellular metabolism.

CLPV:
(b) a heparin-binding protein which, in glycosylated form, has an
apparent
molecular weight of 28 kD, the protein being produced in the
azurophil granules
of polymorphonuclear leukocytes and is capable of binding said
lipid-containing
substance in such a way that, when the conjugate is contacted
with living
cells, the lipid-containing substance activates a
ceramide-activated protein
phosphatase resulting in down-regulation of cellular metabolism.

cells, the lipid-containing substance activates a ceramide-activated protein phosphatase resulting in down-regulation of cellular metabolism.

CCXR:
514/8

good

of interest

see also 5,464,815 of which this is a CON

USPT

US-CL-CURRENT: 514/12,514/21

US-PAT-NO: 5851989
DOCUMENT-IDENTIFIER: US 5851989 A
TITLE: Method of extending the plasma half-life of vascular endothelial cell
growth factor
DATE-ISSUED: December 22, 1998
INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Chamow; Steven	San Mateo	CA	N/A	N/A
Modi; Nishit	San Bruno	CA	N/A	N/A
Schwall; Ralph	Pacifica	CA	N/A	N/A
Zioncheck; Thomas	Montara	CA	N/A	N/A

US-CL-CURRENT: 514/8,514/12 ,514/21
ABSTRACT:
The invention provides a method for extending the plasma half-life of heparin-binding proteins by coadministering such proteins with a therapeutically acceptable compound capable of inhibiting their binding to a low affinity heparin-like binding site on the surface of cells. In one embodiment of the invention, the heparin-binding protein is a growth factor or selectin. The binding inhibitory compound can, for example, be a purified native heparin preparation, a heparin fragment, or another polyanionic compound, such as dextran sulfate, heparan sulfate, pentosan sulfate, or hyaluronate.
14 Claims, 12 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 7

BSPR:
The present invention is based on the finding that the in vivo half-life of heparin-binding growth factors, such as HGF, in the plasma can be significantly

extended by coadministration with a polyanionic molecule, such as heparin or heparin-derived oligosaccharides. It has further been found that the coadministration of polyanionic molecules increases the amount of heparin-binding proteins entering the plasma after intraperitoneal or subcutaneous administration. Although it is believed that the effect of polyanionic molecules on the bioavailability of heparin-binding proteins is due to their ability to block the binding of heparin-binding proteins to extracellular matrix glycosylaminoglycans, the invention is not limited by this or any other theory in any way. The invention is additionally based on the finding that the presence of polyanionic molecules, and specifically heparin and heparin-like oligosaccharides potentiates the biological activity of heparin-binding proteins (HGF, IL-8) and/or enhances their binding to their respective native receptors (VEGF).

DEPR:
A "functional derivative" of a native heparin-binding protein is a compound that retains at least one qualitative biological activity of the corresponding native protein and has the ability to bind heparin. Functional derivatives include, but are not limited to, fragments of native heparin-binding proteins from any animal species, and derivatives of the native proteins and fragments thereof, wherein the term "derivative" is used to define amino acid sequence and glycosylation variants, and covalent modifications of a native protein, whereas the term "variant" refers to amino acid sequence and glycosylation variants within this definition. An "inhibitor" of a native heparin-binding protein is a compound that inhibits at least one biological activity of the corresponding native protein and has the ability to bind heparin.

DEPR:
The term "glycosylation variant" is used to refer to a heparin-binding protein

molecule having a glycosylation profile different from that of a corresponding native protein. Glycosylation of polypeptides is typically either N-linked or O-linked. N-linked refers to the attachment of the carbohydrate moiety to the side-chain of an asparagine residue. The tripeptide sequences, asparagine-X-serine and asparagine-X-threonine, wherein X is any amino acid except proline, are recognition sequences for enzymatic attachment of the carbohydrate moiety to the asparagine side chain. O-linked glycosylation refers to the attachment of one of the sugars N-acetylgalactosamine, galactose, or xylose to a hydroxyamino acid, most commonly serine or threonine, although 5-hydroxyproline or 5-hydroxylysine may also be involved in O-linked glycosylation. Any difference in the location and/or nature of the carbohydrate moieties present in a glycosylation variaty or fragment as compared to its native counterpart is within the scope herein.

DEPR:
The rationale for the use of dextran sulfate is that in a separate series of experiments, we found that premixing of HGF/SF with soluble heparin greatly enhanced its bioavailability from subcutaneous and intraperitoneal sites (unpublished observation). This effect was not specific to heparin and was also observed with other sulfated polysaccharides including pentosan polysulfate, hyaluronate, and dextran sulfate. Dextran sulfate was chosen arbitrarily for the infusion studies. At a 1:10 HGF/SF:dextran sulfate ratio the solution was extremely viscous and probably could not get out of the infusion pump. However, ratios of 1:1 or 1:2 enhanced the effectiveness of HGF/SF infusions. Although the mechanism is not known, we hypothesize that, because HGF/SF binds heparin strongly (Nakamura et al., Proc. Natl. Acad. Sci. USA 83, 6489-6493 [1986]), its absorption from subcutaneous and intraperitoneal sites is low due to trapping by interaction with

heparin
sulfate proteoglycans in the extracellular matrix. We therefore speculate that
sulfated polysaccharides saturate the heparin binding regions on HGF/SF,
thereby preventing interaction with matrix components. Heparin also decreases
the clearance of HGF/SF, and sulfated polysaccharides enhance hepatocyte
responses to low doses of HGF/SF.

CCOR:
514/8

USPT

US-CL-CURRENT: 435/101,514/12 ,514/21 ,514/54 ,530/399 ,530/412 ,530/413
,536/123 ,536/21 ,536/53 ,536/55.3

US-PAT-NO: 5849722
DOCUMENT-IDENTIFIER: US 5849722 A
TITLE: Oligosaccharide having affinity for fibroblast growth factor and
process for producing same
DATE-ISSUED: December 15, 1998
INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Habuchi; Hiroko	Aichi	N/A	N/A	JPX
Suzuki; Sakaru	Aichi	N/A	N/A	JPX
Kimata; Koji	Aichi	N/A	N/A	JPX

US-CL-CURRENT: 514/56,435/101 ,514/12 ,514/21 ,514/54 ,530/399 ,530/412
,530/413 ,536/123 ,536/21 ,536/53 ,536/55.3
ABSTRACT:
An oligosaccharide having an affinity for fibroblast growth factor, which is composed of 8 to 18 monosaccharide residues, wherein a principal disaccharide unit comprising L-iduronic acid 2-sulfate and N-sulfo-D-glucosamine and a process for producing the oligosaccharide comprising digesting heparan sulfate.
8 Claims, 4 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 4

BSPR:
JP-A-2-40399 discloses a complex consisting of glycosaminoglycan

application"). This publication describes that the invention was accomplished
based on a finding that stability of the FGF mutein increases markedly when
glycosaminoglycan such as heparan sulfate and low molecular weight heparan
sulfates prepared using hydrogen peroxide is added to an aqueous solution of
the FGF mutein.

BSPR:
In addition, JP-A-63-66192 (hereinafter referred to as "Sanofi application")
illustrates an invention entitled "Heparin-based Oligosaccharides having
Affinity for Cell Growth Factors". The above invention aims at providing
heparin type or heparan sulfate type oligosaccharides having markedly high
affinities for heparin-binding cell growth factors, which can be obtained, for
example, by a process which comprises the steps of: subjecting natural heparin
or natural heparan sulfate chain which serves as a starting material to
depolymerization (molecular weight reduction) with nitric acid, heparinase,
heparitinase or periodic acid; subjecting the resulting product to alcohol
precipitation for separating a fraction of saccharides having 10 monosaccharide
residues or less and a fraction of saccharides having more than 10
monosaccharide residues; applying the fraction of saccharides having 10
monosaccharide residues or less to an agarose-acrylamide column for separating
into a disaccharide fraction, a tetrasaccharide fraction, a hexasaccharide
fraction, an octasaccharide fraction and a decasaccharide fraction; and
removing chains having no affinity or medium affinity for FGF by

BSPR:
Thus, a complex of the FGF mutein with glycosaminoglycan according to the Sanofi application is composed of the FGF mutein which is not a naturally occurring fibroblast growth factor, because certain amino acids of human basic fibroblast growth factor are replaced with other amino acids. In addition, though it discloses a low molecular weight heparan sulfate as an example of glycosaminoglycan, its illustrative description includes only a complex which consists of the FGF mutein and a relatively long-chained heparin or heparan sulfate. Such a complex possibly might have pharmacologically and physiologically unnecessary or improper structural moieties which react, for example, with antithrombin III, heparin cofactor II, platelet factor 4 and the like.

CCXR:
530/399

USPT

US-CL-CURRENT: 514/2,514/54 ,514/56 ,514/57 ,514/61 ,514/62
,514/8 ,536/123.1
,536/123.13 ,536/21 ,536/56

US-PAT-NO: 5783568
DOCUMENT-IDENTIFIER: US 5783568 A
TITLE: Methods for treating cancer and other cell proliferative
diseases
DATE-ISSUED: July 21, 1998
INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Schlessinger; Joseph	New York	NY	N/A	N/A
Lax; Irit	Fair Lawn	NJ	N/A	N/A
Ladbury; John E.	New York	NY	N/A	N/A
Tang; Peng Cho	Moraga	CA	N/A	N/A

US-CL-CURRENT: 514/53,514/2 ,514/54 ,514/56 ,514/57 ,514/61
,514/62 ,514/8
,536/123.1 ,536/123.13 ,536/21 ,536/56
ABSTRACT:
The present invention relates to a method of treating in a
mammal certain
cancers, other cell proliferative diseases, and/or angiogenesis
by using a salt
or complex of a sulfated saccharide. The invention also relates
to the use of
mutant heparin binding growth factors that bind to the growth
factor receptor,
but not to heparin. The invention also provides pharmaceutical
compositions
for such methods.
9 Claims, 9 Drawing figures
Exemplary Claim Number: 1

not relevant

dimerization and activation of the receptor involved in the condition treated.
Thus, the sulfated compounds inhibit cancer or cell proliferative diseases by
inhibiting the activity of heparin-binding growth factors.

DEPR:
The saccharide component of the sulfated saccharide used in accordance with the
invention is a monosaccharide, for example, xylose, fructose or glucose, an
oligosaccharide, for example, a disaccharide such as sucrose, lactose, maltose
or cellobiose, or maltotriose, maltotetrose, maltopeptose, maltohexose, or
fragments of heparin small enough not to bind more than one heparin-binding
growth factor at a time or a subunit of any of such saccharides.

CCXR:
514/8

USPT

US-CL-CURRENT: 514/21,530/380 ,530/395

US-PAT-NO: 5814602
DOCUMENT-IDENTIFIER: US 5814602 A
TITLE: Heparin-binding proteins
DATE-ISSUED: September 29, 1998
INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Flodgaard; Hans	Hellerup	N/A	N/A	DKX
Ostergaard; Erik	Vanlose	N/A	N/A	DKX
Thomsen; Johannes	Kokkedal	N/A	N/A	DKX
Bayne; Stephen	Roskilde	N/A	N/A	DKX

US-CL-CURRENT: 514/8,514/21 ,530/380 ,530/395

ABSTRACT:
A heparin-binding protein (HBP) which has, in glycosylated state, an apparent molecular weight of about 28 kDa, determined by SDS-PAGE under reducing conditions, and exhibits angiogenic properties in vivo.

10 Claims, 6 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 6

ABPL:
A heparin-binding protein (HBP) which has, in glycosylated state, an apparent molecular weight of about 28 kDa, determined by SDS-PAGE under reducing conditions, and exhibits angiogenic properties in vivo.

CCOR:
514/8

USPT

US-CL-CURRENT: 435/69.1,530/402

US-PAT-NO: 5686572
DOCUMENT-IDENTIFIER: US 5686572 A
TITLE: Domains of extracellular region of human platelet derived growth factor receptor polypeptides
DATE-ISSUED: November 11, 1997
INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Wolf; David	Palo Alto	CA	N/A	N/A
Tomlinson; James E.	San Francisco	CA	N/A	N/A
Fretto; Larry J.	Belmont	CA	N/A	N/A
Giese; Neill A.	San Francisco	CA	N/A	N/A
Escobedo; Jaime A.	San Francisco	CA	N/A	N/A
Williams; Lewis Thomas	Tiburon	CA	N/A	N/A

US-CL-CURRENT: 530/350,435/69.1 ,530/402
ABSTRACT:

Defined constructs of modified human platelet-derived growth factor receptor polypeptides are provided. Extracellular region domain structures are identified and modifications and combinatorial rearrangements of the receptor segments are provided. Both cell bound and soluble forms of modified segments are made available, as are methods for assays using them, allowing for screening of ligand analogues.
8 Claims, 4 Drawing figures

factor receptor
polypeptide. Primary structures of two homologous forms of polypeptides have
been reported. A type B receptor nucleic acid and its corresponding
polypeptide sequence from mouse are reported in Yarden et al. (1986) Nature
323: 226-232; and a homologous genetic sequence has been isolated from humans.
See application Ser. No. 07/771,829 which is a continuation of Ser. No.
07/309,332, now abandoned. A human type A receptor sequence is reported in
Matsui et al. (1989) Science 243: 800-803. Although the two different forms of
the receptor polypeptides are homologous, they are encoded by two separate
genes.

CCXR:
530/402

ORPL:
Daniel et al. (1987) "Biosynthetic and Glycosylation Studies of Cell Surface
Platelet-Derived Growth Factor Receptors" J. Biol. Chem. 262:9778-9784.

ORPL:
Keating et al. (1989) "Platelet-Derived Growth Factor Receptor Inducibility Is
Acquired Immediately after Translation and Does Not Require Glycosylation" J.
Biol. Chem. 264:9129-9132.

USPT

US-CL-CURRENT: 435/69.1,514/21 ,530/350 ,530/389.2 ,530/399

US-PAT-NO: 5686415
DOCUMENT-IDENTIFIER: US 5686415 A
TITLE: Method for the treatment of colon epithelial cells in vivo
DATE-ISSUED: November 11, 1997
INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Carnahan; Josette	Newbury Park	CA	N/A	N/A
Fran.cedilla.oise	Thousand Oaks	CA	N/A	N/A
Hara; Shinichi	Thousand Oaks	CA	N/A	N/A
Lu; Hsieng Sen	Boulder	CO	N/A	N/A
Mayer; John Philip	Thousand Oaks	CA	N/A	N/A
Yoshinaga; Steven Kiyoshi				

US-CL-CURRENT: 514/12,435/69.1 ,514/21 ,530/350 ,530/389.2 ,530/399
ABSTRACT:
Colon epithelial cells are stimulated to multiply, grow and mature by contacting them in vivo with peptides derived from the EGF-like domain of proteins of the NDF/heregulin family.
5 Claims, 8 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 5

BSPR:
The cell membrane-bound precursor forms of these proteins (referred to in this

immunoglobulin(Ig)-like domain
(approximately 70 amino acid residues), a so-called "spacer"
domain that
contains multiple binding sites for N- and O-linked
glycosylation, an epidermal
growth factor (EGF)-like domain of about 60-75 amino acid
residues that
includes 6 cysteine residues, a hydrophobic region of about 25
amino acid
residues that functions as a transmembrane domain, and a
"cytoplasmic tail"
which can vary in length. Some of these transmembranous
precursor forms
undergo proteolytic cleavage in the cell at both the N-terminus
and at the
short stretch of sequence (juxtamembrane) that connects the
EGF-like domain
with the transmembrane domain. Depending on the amino acid
sequence in this
juxtamembrane region, the NDF/heregulins have been designated
subtype 1,
subtype 2, subtype 3, etc. Additional variations comprise two
forms of the
C-terminal loop of the EGF-like domain, which are termed
alpha(.alpha.) and
beta(.beta.), depending on the amino and sequence in this region;
Wen et al.,
Molecular and Cellular Biology, Volume 14, Number 3, pages
1909-1919 (1994).

DRPR:
FIG. 1. This figure is a schematic drawing (not in proportional
scale) of the
extracellular structure of human NDF/heregulin, comprising
(distal from the end
that binds to the cell membrane): the putative N-terminal
"heparin-binding"
region, an immunoglobulin (Ig)-like domain, a carbohydrate (or
"spacer")
domain, and an EGF-like domain proximal to the C-terminal end.
The open
circles in the spacer domain represent O-linked sugars and the

towards the C-terminal end. The EGF-like domain begins approximately at amino
acid residue position 177 (marked) and ends approximately at amino acid residue
position 228 (not marked).

CCXR:
530/399

USPT

US-CL-CURRENT: 435/252.3,435/252.33 ,435/255.1 ,435/320.1 ,435/69.1 ,435/69.4 ,530/399 ,536/23.51

very generic see also 5,360,896 for claims to the glycosylated product. very generic

US-PAT-NO: 5464943
DOCUMENT-IDENTIFIER: US 5464943 A
TITLE: DNA encoding glycosylated FGF and production thereof
DATE-ISSUED: November 7, 1995
INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Senoo; Masaharu	Toyonaka	N/A	N/A	JPX
Sasada; Reiko	Kyoto	N/A	N/A	JPX
Igarashi; Koichi	Kyoto	N/A	N/A	JPX

US-CL-CURRENT: 536/23.5,435/252.3 ,435/252.33 ,435/255.1 ,435/320.1 ,435/69.1 ,435/69.4 ,530/399 ,536/23.51

ABSTRACT:

Disclosed are (1) a mutein of a fibroblast growth factor (FGF), the DNA having introduced therein at least one nucleotide sequence coding for a glycosylation site, (2) a DNA coding for the mutein of (1), (3) a vector containing the DNA of (2), (4) a transformant transformed with the vector of (3), and (5) a process for producing the mutein which comprises cultivating in a culture medium the transformant of a yeast or animal cell transformed with a vector of (3), and producing and accumulating the mutein of (1) in the culture medium, whereby the FGF mutein into which at least one glycosylation site has

the DNA having
introduced therein at least one nucleotide sequence coding for a glycosylation
site, (2) a DNA coding for the mutein of (1), (3) a vector containing the DNA
of (2), (4) a transformant transformed with the vector of (3), and (5) a
process for producing the mutein which comprises cultivating in a culture
medium the transformant of a yeast or animal cell transformed with a vector of
(3), and producing and accumulating the mutein of (1) in the culture medium,
whereby the FGF mutein into which at least one glycosylation site has been
introduced is improved in productivity, stability and activities, and
advantageously used as medicine.

BSPV:
(1) a mutein of a fibroblast growth factor (FGF) into which at least one
glycosylation site has been introduced,

CLPR:
1. A DNA coding for a mutein of a naturally occurring fibroblast growth factor
(FGF), the DNA having artificially introduced therein at least one nucleotide
sequence coding for a glycosylation site which is represented by -Asn-X-Y,
wherein X is Gly, Lys, Val or Ala; Y is Thr, Ser or Cys; subject to the
limitation that -X-Y- is not -Gly-Ser-.

CLPR:
3. A plasmid containing a DNA coding for a mutein of a naturally occurring
fibroblast growth factor (FGF), the DNA having artificially introduced therein
at least one nucleotide sequence coding for a glycosylation site which is

artificially introduced at least one nucleotide sequence coding for a
glycosylation site which is represented by -Asn-X-Y-, wherein X is Gly, LyS,
Val or Ala; Y is Thr, Ser or Cys; subject to the limitation that -X-Y- is not
-Gly-Ser-.

CLPR:
9. A process for producing a mutein of a naturally occurring fibroblast growth
factor (FGF), into which has been artificially introduced at least one
glycosylation site which is represented by -Asn-X-Y-, wherein X is Gly, Lys,
Val or Ala: Y is Thr, Ser or Cys; subject to the limitation that -X-Y- is not
-Gly-Ser- which comprises;

CLPV:
cultivating in a culture medium a yeast or animal cell transformant transformed
with a vector containing a DNA coding for a mutein of a naturally occurring
fibroblast growth factor (FGF), the DNA having introduced therein at least one
nucleotide sequence coding for a glycosylation site which is represented by
-Asn-X-Y-, wherein X is Gly, Lys, Val or Ala; Y is Thr, Ser or Cys; subject
to the limitation that -X-Y- is not -Gly-Ser-, and recovering said mutein from
the culture medium.

CCXR:
530/399

USPT

US-CL-CURRENT: 435/69.1,435/69.4 ,435/69.5 ,530/397

very good

US-PAT-NO: 5360896
DOCUMENT-IDENTIFIER: US 5360896 A
TITLE: Glycosylated FGF
DATE-ISSUED: November 1, 1994
INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Senoo; Masaharu	Osaka	N/A	N/A	JPX
Sasada; Reiko	Kyoto	N/A	N/A	JPX
Igarashi; Koichi	Kyoto	N/A	N/A	JPX

US-CL-CURRENT: 530/399,435/69.1 ,435/69.4 ,435/69.5 ,530/397
ABSTRACT:

Disclosed are (1) a mutein of a fibroblast growth factor (FGF), the DNA having introduced therein at least one nucleotide sequence coding for a glycosylation site, (2) a DNA coding for the mutein of (1), (3) a vector containing the DNA of (2), (4) a transformant transformed with the vector of (3), and (5) a process for producing the mutein which comprises cultivating in a culture medium the transformant of a yeast or animal cell transformed with a vector of (3), and producing and accumulating the mutein of (1) in the culture medium, whereby the FGF mutein into which at least one glycosylation site has been introduced is improved in productivity, stability and activities, and advantageously used as medicine.

16 Claims, 19 Drawing figures

containing the DNA
of (2), (4) a transformant transformed with the vector of (3), and (5) a
process for producing the mutein which comprises cultivating in a culture
medium the transformant of a yeast or animal cell transformed with a vector of
(3), and producing and accumulating the mutein of (1) in the culture medium,
whereby the FGF mutein into which at least one glycosylation site has been
introduced is improved in productivity, stability and activities, and
advantageously used as medicine.

BSPV:
(1) a mutein of a fibroblast growth factor (FGF) into which at least one
glycosylation site has been introduced,

CLPR:
1. A mutein of a naturally occurring fibroblast growth factor (FGF) into which
has been artificially introduced at least one glycosylation site which is
represented by -Asn-X-Y-, wherein X is Gly, Lys, Val or Ala; Y is Thr, Ser or
Cys; subject to the limitation that -X-Y- is not -Gly-Ser-.

CLPR:
12. The mutein according to claim 1, wherein the mutein is produced from a DNA
coding for a mutein of a fibroblast growth factor (FGF), the DNA having
artificially introduced therein at least one nucleotide sequence coding for the
glycosylation site.

CCOR:
530/399

USPT

US-CL-CURRENT: 514/54,514/56 ,514/59 ,514/885 ,514/886 ,514/889 ,530/399

US-PAT-NO: 5288704
DOCUMENT-IDENTIFIER: US 5288704 A
TITLE: Synergistic composition comprising a fibroblast growth factor and a sulfated polysaccharide, for use as antiviral agent
DATE-ISSUED: February 22, 1994
INVENTOR-INFORMATION:

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Carminati; Paolo	Milan	N/A	N/A	ITX
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US-CL-CURRENT: 514/12,514/54 ,514/56 ,514/59 ,514/885 ,514/886 ,514/889 ,530/399

ABSTRACT:
A pharmaceutcial composition is provided for use in the prevention or treatment of viral infections caused by enveloped viruses. The composition comprises a fibroblast growth factor, a sulfated polysaccharide with antiviral activity, and one or more pharmaceutically acceptable carriers. The fibroblast growth factor may be a basic fibroblast growth factor or an analogue thereof, and the polysaccharide may be a carrageenan, heparin, dextran

Synergistic composition comprising a fibroblast growth factor and a sulfated
polysaccharide, for use as antiviral agent

ABPL:
A pharmaceutcial composition is provided for use in the prevention or treatment
of viral infections caused by enveloped viruses. The composition comprises a
fibroblast growth factor, a sulfated polysaccharide with antiviral activity,
and one or more pharmaceutically acceptable carriers. The fibroblast growth
factor may be a basic fibroblast growth factor or an analogue thereof, and the
polysaccharide may be a carrageenan, heparin, dextran sulfate, pentosan
polysulfate or a sulfated polysaccharides produced by marine algae belonging to
the class of Rhodophyceae.

BSPR:
The present invention relates to a synergistic pharmaceutical composition
having antiviral activity which comprises a fibroblast growth factor, a
sulfated polysaccharide with antiviral activity and any acceptable
pharmaceutical excipient or excipients, for the use in the prevention or
treatment of viral infections caused by enveloped viruses.

BSPR:
We have surprisingly found that combining a fibroblast growth factor and a
sulfated polysaccharide, the obtained antiviral activity is superior to that
expected from the sum of the antiviral activities of the individual
constituents of the combination, thus indicating the presence of a synergistic
effect. The combination of the two components is therefore more

acceptable
pharmaceutical excipient or excipients, for use in the prevention
or treatment
of viral infections caused by enveloped viruses.

DRPR:
The invention further concerns a process for preparing the above
mentioned
composition, comprising the step of combining a fibroblast growth
factor, and a
sulfated polysaccharide in a pharmaceutically acceptable
excipient or
excipients.

CCXR:
530/399